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No. 95-1275

In the Supreme Court of the United States

OCTOBER TERM, 1995

JENNIE R. LEFEVRE, SALLY M. HILL, FREDERICK L. RADA, AND MARY CHRISTINA VELDMAN, PETITIONERS

v.

JESSE BROWN, SECRETARY OF VETERANS AFFAIRS

ON PETITION FOR A WRIT OF CERTIORARI TO THE UNITED STATES COURT OF APPEALS FOR THE FEDERAL CIRCUIT

BRIEF FOR THE RESPONDENT IN OPPOSITION

DREW S. DAYS, III
Solicitor General

MARY LOU KEENER
General Counsel

RICHARD J. HIPOLIT
Deputy Assistant General Counsel

DAVID J. BARRANS
Attorney
Department of Veterans Affairs
Washington, D.C. 20420

FRANK HUNGER
Assistant Attorney General

JOHN F. DALY
HENRY A. AZAR, JR.
Attorneys

Department of Justice
Washington, D.C. 20530
(202) 514-2217

QUESTIONS PRESENTED

1. Whether, in upholding the decision of the Secretary of Veterans Affairs under the Agent Orange Act of 1991 (Act), Pub. L. No. 102-4, 105 Stat. 11, 38 U.S.C. 1116, not to establish a presumption of a connection between prostate cancer in Vietnam veterans and service in Vietnam, the court of appeals relied on a ground that was not relied upon by the Secretary.

2. Whether the Act required the Secretary to discuss the possible existence of biologically plausible mechanisms by which exposure to herbicides or substances found therein is associated with hepatobiliary and nasal/nasopharyngeal cancers.

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OPINIONS BELOW

The opinion of the court of appeals (Pet. App. 1a-27a) is reported at 66 F.3d 1191. The decision of the Secretary of Veterans Affairs (Pet. App. 28a-45a) is published at 59 Fed. Reg. 341.

JURISDICTION

The judgment of the court of appeals was entered on September 15, 1995. A petition for rehearing was denied on October 13, 1995. Pet. App. 46a. On December 12, 1995, the Chief Justice extended the time within which to file a petition for a writ of certiorari to and including February 12, 1996, and the petition was filed

on that date. The jurisdiction of this Court is invoked under 28 U.S.C. 1254(1).

STATEMENT

1. The Agent Orange Act of 1991 (Act), Pub. L. No. 102-4, 105 Stat. 11, 38 U.S.C. 1116, requires the Secretary of Veterans Affairs to establish a presumption of service connection for diseases positively associated with exposure to Agent Orange and other herbicides used in Vietnam. Such a presumption means that, as to all veterans who served in Vietnam and who develop that disease within the time period, if any, prescribed by statute or regulation, the disease "shall be considered to have been incurred in or aggravated by such service." 38 U.S.C. 1116(a)(1). Veterans disabled by presumptively service-connected diseases are generally entitled to benefits, see 38 U.S.C. 1110; 38 C.F.R. 3.303, as are the surviving spouses, parents, and minor children of veterans who die from such diseases, see 38 U.S.C. 1310-1311.

Under the Act, the Secretary must establish a presumption of service connection when he finds a "positive association" between the occurrence of a disease in humans and exposure to a herbicide agent. 38 U.S.C. 1116(b)(1). A "positive association" exists when "the credible evidence for the association is equal to or outweighs the credible evidence against the association." 38 U.S.C. 1116(b)(3). The Act directs the Secretary, in determining whether a positive association exists, to consider "sound medical and scientific evidence." 38 U.S.C. 1116(b)(1). In addition, the Act specifically directs the Secretary to take into account reports of the National Academy of Sciences (NAS or Academy). 38 U.S.C. 1116(b)(2).

To provide for the NAS reports, the Act directs the Secretary to seek to enter into a contract with the NAS to review and summarize the scientific evidence. Act § 3(b) and (c), 105 Stat. 13. The Act provides that, under the contract, the NAS must determine for each disease it considers (1) whether a statistical association exists between herbicide exposure and the disease; (2) whether there is an increased risk of the disease among those who were exposed to herbicides in Vietnam; and (3) whether a plausible biological mechanism exists between herbicide exposure and the disease. Act § 3(d)(1), 105 Stat. 13. The NAS also must "include in its reports * * * a full discussion of the scientific evidence and reasoning that led to its conclusions" concerning those three issues. Act § 3(d)(2), 105 Stat. 14. The NAS is required under the contract prescribed by the Act to submit its reports at least once every two years after the date of the first report. Act § 3(g), 105 Stat. 14.

Within 60 days after receiving a report from the NAS, the Secretary must determine whether a presumption of service connection is warranted for each disease discussed in the report. 38 U.S.C. 1116(c)(1)(A) and (B). If he determines that a presumption of service connection is warranted for a disease, he must issue regulations consistent with that determination. 38 U.S.C. 1116(c)(1)(A) and (c)(2). If he determines that a presumption of service connection is not warranted for a disease, he must, within 60 days of making that determination, publish a notice of that determination in the Federal Register, including an explanation of the scientific basis for the determination. 38 U.S.C. 1116(c)(1)(B).

2. In July 1993, the NAS issued its first report, *Veterans and Agent Orange: Health Effects of Her-*

bicides Used in Vietnam (Report). Pet. App. 30a. The NAS based its Report on a review of approximately 6,420 abstracts of scientific or medical articles, approximately 230 of which were selected for detailed analysis. *Ibid.* The NAS also held public meetings and consulted with outside experts. *Ibid.* In accordance with the Academy's statutorily prescribed contract obligations, the Report discussed, for each disease covered, any statistical association between the disease and herbicides; any increased risk of the disease among Vietnam veterans exposed to herbicides; and any biologically plausible mechanism between herbicide exposure and the disease. See Act § 3(d)(2), 105 Stat. 14.

As to the first issue, the Report assigned each of 31 diseases to one of four categories, depending on the strength of the evidence of a statistical association between that disease and herbicide exposure. Pet. App. 5a. The four categories, in descending order of strength of evidence, are "Sufficient Evidence of an Association," "Limited/Suggestive Evidence of an Association," "Inadequate/Insufficient Evidence to Determine Whether an Association Exists," and "Limited/Suggestive Evidence of No Association." *Id.* at 5a-6a.[1] As to the three diseases at issue here,

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[1] The two categories relevant here are defined as follows (Pet. App. 5a):

> Limited/Suggestive Evidence of an Association: Evidence is suggestive of an association between herbicides and the outcome but is limited because chance, bias, and confounding could not be ruled out with confidence. For example, at least one high-quality study shows a positive association, but the results of other studies are inconsistent.

the NAS placed prostate cancer in the Limited/Suggestive Evidence of an Association category, *id.* at 5a, and hepatobiliary (liver) cancers and nasal/nasopharyngeal (nose) cancers in the Inadequate/Insufficient Evidence category, *id.* at 6a. The NAS noted that its categorization of diseases "is not intended to imply or suggest any policy decisions, which must rest with the Secretary." *Ibid.*

The Report also discussed the issue of increased risk to Vietnam veterans exposed to the herbicides. Pet. App. 6a. With respect to each disease at issue here, the Academy determined that "it [was] not possible * * * to quantify the degree of risk likely to have been experienced by Vietnam veterans because of their exposure to herbicides in Vietnam." *Ibid.*

The Report used information from tests on animals and information on human exposure to herbicides to determine the biological plausibility for health effects observed in humans. C.A. App. 110. The NAS considered biological plausibility with respect to four herbicides used in Vietnam: 2,4-dichlorophenoxyacetic acid (2,4-D); 2,4,5-trichlorophenoxyacetic acid (2,4,5-T); picloram; and cacodylic acid. C.A. App. 107.[2] In addition, the NAS considered biological plausibility with respect to 2,3,7,8-tetrachlorodibenzo-*p*-dioxin (TCDD or dioxin), which is an unavoidable

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Inadequate/Insufficient Evidence to Determine Whether an Association Exists: The available studies are of insufficient quality, consistency, or statistical power to permit a conclusion regarding the presence or absence of an association. For example, studies fail to control for confounding, have inadequate exposure assessment, or fail to address latency.

[2] Agent Orange, the most extensively used herbicide in Vietnam, consisted of equal amounts of the *n*-butyl esters of 2,4-D and 2,4,5-T. C.A. App. 106H.

contaminant of 2,4,5-T. *Ibid.* The NAS concluded that there was "as yet no convincing evidence of, or mechanistic basis for, the carcinogenicity of any of the herbicides used in Vietnam." Pet. App. 6a (quoting NAS Report). The NAS found extensive evidence, however, that dioxin causes cancer in laboratory animals. *Id.* at 7a.

3. The VA convened the VA Agent Orange Task Force to analyze the Report from a medical and scientific perspective and to solicit comments from veterans service organizations. Pet. App. 7a. After doing so, the Task Force recommended establishing a presumption of service connection for seven diseases, but recommended against establishing such a presumption for the three diseases at issue here. Pet. App. 7a-8a. The Task Force also recommended that special attention be paid to prostate cancer in the next NAS report. *Ibid.*

In September 1993, the Secretary informed the Chairman of the Senate Committee on Veterans Affairs that he had approved the Task Force's recommendations as to which diseases merited a presumption of service connection. C.A. App. 289. The Secretary also informed the Chairman that he was asking the NAS to focus on prostate cancer in its next report. Pet. App. 8a.

In January 1994, the Secretary announced his determination that a presumption of service connection was not warranted for 20 diseases, including the three at issue here. Pet. App. 28a-45a. He observed that, although the Act requires him to base his findings on "credible evidence," it does not define "credible." He therefore turned to the statutory criteria for evaluating studies set forth in 38 U.S.C. 1116(b)(2). He determined that it is not valid to assess

the overall weight of the evidence merely by comparing the number of studies showing a positive statistical association between a disease and herbicide exposure to the number of studies showing a negative statistical association in that regard. Pet. App. 29a-30a. He explained that it is also necessary to determine the credibility of each study, and therefore the weight to be accorded it, by considering factors such as statistical significance, confidence levels, and control for confounding factors. *Id.* at 30a. Based on those factors, the Secretary found that the credible evidence against an association between the three diseases at issue here and herbicide exposure outweighed the credible evidence for such an association. Pet. App. 31a-32a (prostate cancer), 33a-34a (liver cancer), 43a-44a (nose cancer). He therefore determined that a positive association does not exist with respect to those three cancers. *Ibid.*[3]

4. Petitioners are a Vietnam veteran with prostate cancer and three widows of Vietnam veterans who died of liver or nose cancer. Before commencing this action, petitioners applied to the Secretary for benefits, alleging that the cancers were caused by the veterans' exposure to herbicides in Vietnam. Pet. App. 8a. While those applications were pending, petitioners filed a petition for review of the Secretary's decision on the First NAS Report in the United States Court of Appeals for the Federal Circuit. As an initial matter, the court held that it had jurisdiction to review the Secretary's decision under

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[3] The Secretary did, however, establish presumptions of service connection for Hodgkin's disease and porphyria cutanea tarda, 59 Fed. Reg. 5,106-5,107 (1994), and for multiple myeloma and respiratory cancers, *id.* at 29,723-29,724 (1994).

38 U.S.C. 502. Pet. App. 9a-14a. That provision authorizes the Federal Circuit to review certain decisions of the Secretary "in accordance with" the judicial review provisions of the Administrative Procedure Act (APA), 5 U.S.C. 701 *et seq.* 38 U.S.C. 502.

Applying APA principles of judicial review, the court of appeals affirmed the Secretary's decision. Pet. App. 14a-27a. It rejected petitioners' argument that the Secretary "did not give sufficient weight" to the evidence of a positive association between the three types of cancer at issue and herbicide exposure. *Id.* at 16a. The court declined to "reweigh the evidence." *Ibid.* The court found that the Secretary "did not uncritically accept or merely rubber-stamp the Academy's factual findings"; instead, the VA Task Force and the Secretary himself independently examined each disease at issue. *Ibid.* The court rejected petitioners' contention that the Secretary's determination regarding prostate cancer was rendered arbitrary and capricious by his mistakenly citing three studies that did not support one of the assertions underlying that determination, instead of citing other studies, cited elsewhere in his decision, that did support the assertion. *Id.* at 21a-22a. The court also held that the Act did not require the Secretary to discuss the issue of biological plausibility in his decision. *Id.* at 19a-20a.

5. In March 1996, after the court of appeals' decision, the NAS issued its second report, *Veterans and Agent Orange: Update 1996* (Second NAS Report). The Second NAS Report focuses on prostate, liver, and nose cancers, among other matters. See Second NAS Report 1-1 to 1-2 (App., *infra*, 3a). The NAS again places prostate cancer in the Limited/Suggestive Evidence of an Association category,

and liver and nose cancers in the Inadequate/ Insufficient Evidence category. Second NAS Report 1-5 (App., *infra*, 7a-8a).

ARGUMENT

Applying the familiar "arbitrary and capricious" standard of review, the court of appeals correctly upheld the decision of the Secretary of Veterans Affairs under the Agent Orange Act of 1991 not to establish a presumption of service connection for prostate cancer, liver cancer, or nose cancer. Petitioners contend, however, that the court of appeals erred by sustaining the Secretary's decision as to prostate cancer on a ground upon which the Secretary did not rely. They also contend that the Act required the Secretary to discuss the possible existence of biologically plausible mechanisms by which exposure to herbicides or to substances found therein is associated with liver and nose cancers. Neither argument has merit or presents an issue of broad importance warranting review by this Court.

1. a. Petitioners argue (Pet. 15-27) that the Secretary erred in declining to establish a presumption of service connection for prostate cancer because, in explaining that determination, he erroneously cited three studies that did not support one of the assertions underlying that determination, instead of two other studies that did support the assertion. Based on that argument, petitioners contend that the court of appeals should have invalidated the Secretary's decision concerning prostate cancer as "arbitrary." Pet. 17. While a reviewing court, in applying the "arbitrary and capricious" standard, "must judge the propriety of [agency] action solely by the grounds invoked by the agency," *SEC* v. *Chenery*

Corp., 332 U.S. 194, 196 (1947) (*Chenery II*), the court will "uphold a decision of less than ideal clarity if the agency's path may reasonably be discerned," *Bowman Transportation, Inc.* v. *Arkansas-Best Freight System*, 419 U.S. 281, 286 (1974). See, *e.g.*, *Shepard* v. *NLRB*, 459 U.S. 344, 350-352 (1983). Because the court of appeals was able to discern the path taken in the Secretary's decision, it did not violate the *Chenery* rule in upholding that decision.

As an initial matter, petitioners err in asserting (Pet. 13) that the "substitution of the Federal Circuit's judgment for that of the agency is clear on the face of the court's opinion." To the contrary, the court expressly recognized that its role was "'not to substitute [its] judgment for that of the' Secretary." Pet. App. 16a (quoting *Motor Vehicle Mfrs. Ass'n* v. *State Farm Mutual Ins. Co.*, 463 U.S. 29, 43 (1983)). Thus, the court properly considered "whether the Secretary has 'examine[d] the relevant [facts] and articulate[d] a[n] [adequate] explanation for [his] action including a rational connection between the facts found and the choice made.'" Pet. App. 16a (quoting *Motor Vehicles Mfrs.*, 463 U.S. at 43) (internal quotation marks omitted, and some bracketed material added, by court below). The court was therefore plainly aware of its limited role in reviewing the Secretary's decision.

The court performed that role appropriately here. First, it determined, as the Secretary had acknowledged in his brief, that he "erred in citing the Fingerhut, Manz, and Saracci studies as supporting the statement that '[t]here are statistically significant occupational studies which show no association between prostate cancer and herbicide exposure.'" Pet. App. 21a. As the court explained, those three

studies actually show a positive association, but are not statistically significant. *Ibid.* The court correctly observed, however, that the Secretary's statement was "not inaccurate[,]" and "would have been accurately supported" if the Secretary had cited to the Ronco and Wiklund studies. *Ibid.* The Ronco and Wiklund studies "*were* statistically significant and showed a negative association and none at all, respectively." *Ibid.* (emphasis added). Those two studies were cited repeatedly elsewhere in the Secretary's decision, see Pet. App. 34a, 35a, 36a, 43a, as well as in the First NAS Report, see C.A. App. 219. Moreover, the Secretary did not preclude reliance on those studies in making his determination regarding prostate cancer, because he used an "e.g." signal to introduce the mistaken citation.[4]

On this record—where there was substantial evidence to support the Secretary's statement and the citation did not exclude that evidence—the Federal Circuit correctly held that the miscitation of the three studies was not a basis for remanding the Secretary's decision. Where a court can discern in the agency's decision "a rational basis for its treatment of the evidence, * * * the 'arbitrary and capricious' test does not require more." *Bowman Transportation*, 419 U.S. at 290; see also 5 U.S.C. 706 (on judicial review under APA, "the court shall review the whole record or those parts of it cited by a

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[4] Petitioners overstate matters when they refer to the miscited studies as "stand[ing] for exactly the opposite principle from that for which the Secretary cites them." Pet. 16. As explained in the text, those studies are not statistically significant, Pet. App. 21a, and thus offered only limited support for a positive association.

party, and due account shall be taken of the rule of prejudicial error").

b. Petitioners' claim (Pet. 13) that the D.C. Circuit would have applied the *Chenery* rule differently than the Federal Circuit did in this case is refuted by *American Legion* v. *Derwinski*, 54 F.3d 789 (D.C. Cir. 1995), cert. denied, 116 S. Ct. 697 ((1996). The petitioners there argued that the Secretary had discontinued a study concerning exposure to Agent Orange under the wrong statutory standard. 54 F.3d at 798. The D.C. Circuit, citing *Chenery II* and *Bowman Transportation*, stated that, "even if some of the agency's remarks might appear erroneous when read in isolation, the court will uphold agency action that, [c]onsidered in its entirety, is based on appropriate considerations and otherwise complies with relevant statutes and the [APA]." *Ibid.* (internal quotation marks omitted). When the court examined the record, it found that, "notwithstanding the Secretary's unfortunate choice of some words," his decision could not be "fairly understood without regard to the supporting materials on which he relied in making his decision." *Id.* at 799. Based on that material, the court concluded that the Secretary had acted appropriately. *Ibid.* Like *American Legion*, this case is one in which the reviewing court was able to discern the agency's rationale without the need for a remand.

Petitioners' broader claim (Pet. 19-23) that the Federal Circuit has systematically disregarded the *Chenery* rule is likewise refuted by the case law. For example, in a case decided only a few months before the decision below, the Federal Circuit refused to uphold a decision of the International Trade Administration, stating: "We are powerless to affirm an

administrative action on a ground not relied upon by the agency." *NEC Home Electronics, Ltd.* v. *United States*, 54 F.3d 736, 743 (1995) (citing *Chenery II*). The Federal Circuit has likewise demonstrated fidelity to the *Chenery* rule in reviewing other decisions of the Administration, see *Ad Hoc Comm.* v. *United States*, 13 F.3d 398, 401 n.8 (citing *Chenery II*), cert. denied, 115 S. Ct. 67 (1994); *U.H.F.C. Co.* v. *United States*, 916 F.2d 689, 700 (1990); *Timken Co.* v. *United States*, 894 F.2d 385, 389 (1990), as well as the decisions of other agencies, see *Doty* v. *United States*, 53 F.3d 1244, 1252 (1995); *Heyl & Patterson, Inc.* v. *O'Keefe*, 986 F.2d 480, 484 (1993); *Acerno* v. *Department of Health & Human Servs.*, 815 F.2d 680, 685-686 (1987); *In re Hounsfield*, 699 F.2d 1320, 1324 (1983). Thus, the two decisions that petitioners describe as inconsistent with the *Chenery* rule, one of which was decided by the Federal Circuit's predecessor, are at most aberrational. See Pet. 19-23 (discussing *Sealed Air Corp.* v. *United States ITC*, 645 F.2d 976 (C.C.P.A. 1981), and *Ward* v. *MSPB*, 981 F.2d 521 (Fed. Cir. 1992)).[5]

c. Practical considerations also weigh against further review of petitioners' *Chenery* argument. In March 1996, the NAS issued its Second Report. See Act § 3(g), 105 Stat. 14. The Second NAS Report focuses on prostate cancer, among other matters (see

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[5] Although petitioners repeatedly refer (*e.g.*, Pet. 23 & n.19, 26) to the exclusivity of the Federal Circuit's jurisdiction over certain types of cases, that exclusivity does not support further review of the *Chenery* issue, since all of the federal courts are bound by the *Chenery* rule and have occasion to apply it. Cf. *Cardinal Chem. Co.* v. *Morton Int'l, Inc.*, 113 S. Ct. 1967, 1971 (1993) (Federal Circuit's ruling bore on its exclusive patent jurisdiction).

Second NAS Report 1-1 to 1-2 (App., *infra*, 3a)), as the Secretary had requested (see Pet. App. 8a). In discussing prostate cancer, the Second Report refers to the same three studies that the Secretary concededly miscited in the decision at issue here. Second Report 7-42 (App., *infra*, 10a). The Secretary thus has an opportunity to correct his erroneous citation in considering the Second Report, and, given his acknowledgement of the error, there is every reason to believe that he will do so. That prospect significantly diminishes the practical importance of the *Chenery* issue, even if we assume, *arguendo*, that it otherwise had merit.

2. Petitioners also contend that the court of appeals erred in affirming the Secretary's decision as to nose and liver cancers because the Secretary did not discuss the evidence of any biologically plausible mechanisms for an association between dioxin exposure and those diseases. Pet. 27-30. In petitioners' view, "the court held, in effect, that the Secretary could ignore" such evidence. Pet. 27. That was neither the actual nor the "effect[ive]" holding of the court of appeals. The fact that the Secretary did not specifically *discuss* biologic plausibility does not mean that he did not *consider evidence* on that issue. Thus, the court's affirmance of the Secretary's decision does not imply that he was free to ignore such evidence. Instead, the court correctly held only that the Secretary was not required to discuss biologic plausibility. See Pet. App. 19a-20a.

As the court of appeals observed, the Act does not, by its terms, require the Secretary to discuss biologic plausibility. Pet. App. 19a. Petitioners argued that, because the Act does require the *Academy* to discuss biologic plausibility, it implicitly imposes a

similar requirement on the *Secretary*. See *ibid.* As the court of appeals explained, however, petitioners had it backwards: "The fact that the 1991 Act expressly required the Academy to consider biologic plausibility but did not impose a similar requirement on the Secretary is a strong indication that the latter was *not* required to do so." *Ibid.* (citing *Russello* v. *United States*, 464 U.S. 16, 23 (1983)) (emphasis added). As the court further explained, that indication is reinforced by the fact that "the Act specified in detail exactly what were the precise duties of the Academy and the Secretary, and provided specific standards for each of them to follow." Pet. App. 19a.

Nor was the Secretary required to discuss biologic plausibility by virtue of the Act's general requirements that, in determining whether to establish a presumption of service connection for a disease, he must consider "sound medical and scientific evidence" (38 U.S.C. 1116(b)(1)), and that, in announcing a decision not to establish such a presumption, he must "include an explanation of the scientific basis for that determination" (38 U.S.C. 1116(c)(1)(B)). In arguing to the contrary, petitioners place far too much weight on the indication of biologic plausibility noted by the Academy. The Academy explained the pertinence of biologic plausibility as follows (C.A. App. 110):

> Information from tests in laboratory animals and other nonhuman systems is useful because it can be combined with information obtained from humans exposed to the herbicides * * * to determine the biologic plausibility for health effects observed in humans * * *. Establishing the biologic plausibility of effects due to herbicide exposure in the laboratory strengthens the

evidence for any effects of the herbicides that are suspected to occur in humans.

Thus, the existence of a biologically plausible mechanism by which herbicide exposure may be associated with a disease can confirm the existence of an association reflected in epidemiological statistics. Indication of a plausible mechanism does not by itself, however, constitute such a strong indication of a positive association that the Secretary was required to address it specifically.

Moreover, the indication of a plausible mechanism that the Academy noted, and upon which petitioners rely, is of only attenuated value here because it concerned not the herbicides themselves, but dioxin, a contaminant of the herbicide 2,4,5-T. C.A. App. 110. As to the herbicides themselves, the Academy found that "there is as yet no convincing evidence of, or mechanistic basis for, the carcinogenicity of any of the herbicides used in Vietnam." Pet. App. 19a. In light of that finding, the Secretary had the discretion not to address biologic plausibility.[6]

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[6] Petitioners assert that "[t]he premise for the court's rulng [*sic*] appears to have been that in making 'positive association' determinations under the Agent Orange Act, the Secretary was only legally obligated to consider sound scientific evidence of association between 'herbicide exposure' and disease, *not* such evidence of association between an 'herbicide contaminant,' *i.e.*, dioxin, and disease." Pet. 27. Based on that assertion, petitioners argue that the Secretary was obligated to consider biologic plausibility as to dioxin because dioxin is a "herbicide agent" within the meaning of the Act (38 U.S.C. 1116(a)(4)). Pet. 27-28. Both steps of petitioners' argument are flawed. As discussed in the text, and contrary to petitioners' assertion, the court of appeals did not rule that the Secretary was free to ignore evidence concerning dioxin. Moreover, although dioxin is a herbicide contaminant, petitioners' conten-

The narrow scope of petitioners' challenge should be emphasized. The Secretary based his determination regarding liver and nose cancers on the Academy's survey of the existing epidemiological studies, which, in the aggregate, did not support a positive association between exposure to herbicides and those cancers. See Pet. App. 33a-34a, 43a-44a. Moreover, the Secretary repeatedly cited epidemiological studies involving exposure to dioxin. *Id.* at 31a, 36a, 39a, 40a, 41a, 42a, 43a. Petitioners therefore do not, and cannot, dispute that the Secretary took dioxin exposure into account in making his determinations. Moreover, although petitioners challenged the Secretary's weighing of the epidemiological studies in the court of appeals (Pet. App. 23a-26a), they do not do so in this Court. They merely challenge the Secretary's failure specifically to discuss one facet of the dioxin evidence. That factbound challenge does not warrant further review.

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tion that it is also a "herbicide agent" under the Act is dubious in light of the Act's reference to "an herbicide agent *containing* dioxin" (38 U.S.C. 1116(a)(3) (emphasis added)), which implies that dioxin is not, itself, a "herbicide agent."

CONCLUSION

The petition for a writ of certiorari should be denied.

Respectfully submitted.

DREW S. DAYS, III
Solicitor General

MARY LOU KEENER
General Counsel

FRANK HUNGER
Assistant Attorney General

RICHARD J. HIPOLIT
Deputy Assistant General Counsel

JOHN F. DALY
HENRY A. AZAR, JR.
Attorneys

DAVID J. BARRANS
Attorney
Department of Veterans Affairs

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APPENDIX

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VETERANS AND AGENT ORANGE: UPDATE 1996

Committee to Review the Health Effects in Vietnam Veterans of Exposure to Herbicides

Division of Health Promotion and Disease Prevention

INSTITUTE OF MEDICINE

IOM

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Executive Summary

Because of continuing uncertainty about the long-term health effects of exposure to herbicides used in Vietnam, Congress passed Public Law 102-4, the "Agent Orange Act of 1991." This legislation directed the Secretary of Veterans Affairs to request the National Academy of Sciences (NAS) to conduct a comprehensive review and evaluation of scientific and medical information regarding the health effects of exposure to Agent Orange, other herbicides used in Vietnam, and the various chemical components of these herbicides, including dioxin. The Institute of Medicine (IOM) of the NAS conducted this review and in 1994 published a comprehensive report, entitled *Veterans and Agent Orange: Health Effects of Herbicides Used in Vietnam* (IOM, 1994).

Public Law 102-4 also called for the NAS to conduct subsequent reviews at least every two years for a period of ten years from the date of the first report. The NAS was instructed to to [*sic*] conduct a comprehensive review of the evidence that has become available since the previous IOM committee report; and reassess its determinations and estimates of statistical association, risk, and biological plausibility.

This IOM report presents the first updated review and evaluation of the newly published scientific evidence regarding associations between diseases and exposure to dioxin and other chemical compounds in herbicides used in Vietnam. For each disease, the

IOM was asked to determine, to the extent that available data permitted meaningful determinations: 1) whether a statistical association with herbicide exposure exists, taking into account the strength of the scientific evidence and the appropriateness of the statistical and epidemiological methods used to detect the association; 2) the increased risk of the disease among those exposed to herbicides during Vietnam service; and 3) whether there is a plausible biological mechanism or other evidence of a causal relationship between herbicide exposure and the disease.

In addition to bringing the earlier scientific evidence up to date, the committee has addressed several specific areas of concern, as requested by the Department of Veterans Affairs (DVA). These are: 1) the relationship between exposure to herbicides and the development of acute and subacute peripheral neuropathy; 2) the relationship between exposure to herbicides and the development of [1-2] prostate cancer, hepatobiliary cancer, and nasopharyngeal cancer; and 3) the relationship between the length of time since first exposure and the possible risk of cancer development.

In conducting its study, the IOM committee operated independently of the DVA and other government agencies. The committee was not asked to and did not make judgments regarding specific cases in which individual Vietnam veterans have claimed injury from herbicide exposure. Rather, the study provides scientific information for the Secretary of Veterans Affairs to consider as the DVA exercises its responsibilities to Vietnam veterans.

ORGANIZATION AND FRAMEWORK

The conclusions in this updated report are based on cumulative evidence from the scientific literature reviewed in *Veterans and Agent Orange: Health Effects of Herbicides Used in Vietnam*, which will be abbreviated here as *VAO*. This update is intended to supplement rather than replace *VAO*; therefore, most of the background information has not been repeated. Most chapter sections begin with brief summaries of the scientific data in *VAO*, followed by a more thorough discussion of the newly published data and their interpretation. The reader is referred to relevant sections of *VAO* for additional detail and explanation.

Chapter 2 provides an overview of the methods and conclusions *VAO* [*sic*]. In addition, it provides a summary of the recent activities of several federal government agencies that are relevant to the health effects of Agent Orange and other herbicides used in Vietnam. Chapter 3 provides an update of the recent experimental toxicology date on the effects of the herbicides and of TCDD, a compound found as a contaminant in the herbicide 2,4,5-trichlorophenoxyacetic acid (2,4,5-T). These data serve as the basis for the biological plausibility of potential health effects in human populations. Chapter 4 describes the methodological considerations that guided the committee's review and its of [sic] evaluation. Chapter 5 updates the exposure assessment issues in *VAO* Chapter 8[,] reviews the methods used to study latency, or time-related effects—a topic of special interest to the DVA—and evaluates the evidence on latency for the cancers under study.

The committee focused most of its efforts on reviewing and interpreting epidemiologic studies, in

order to judge whether each of the human health effects is associated with exposure to herbicides or dioxin. The committee weighed the strengths and limitations of the scientific data in *VAO* as well as the newly published scientific data, and reached its conclusions by interpreting the new evidence in the context of the original report. In particular, each disease has been placed into one of four categories, depending on the strength of evidence for an association (see Conclusions about Health Outcomes, below). The committee used the same criteria to categorize diseases as were used in *VAO*.

In the chapters on the various health outcomes (7, 9, 10, and 11), the committee relied on many of the same epidemiologic studies when assessing the potential associations with herbicides. Therefore, Chapter 6 provides a framework for the methods used in the epidemiologic studies. The chapter is organized to reflect similarities and differences in the nature of exposure among three types of study populations: occupationally exposed, environmentally exposed, and Vietnam veterans.

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TABLE 1-1 Updated Summary of Findings in Occupational, Environmental, and Veterans Studies Regarding the Association Between Specific Health Problems and Exposure to Herbicides

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Sufficient Evidence of an Association

Evidence is sufficient to conclude that there is a positive association. That is, a positive association has been observed between herbicides and the out-

come in studies in which chance, bias, and confounding could be ruled out with reasonable confidence. For example, if several small studies that are free from bias and confounding show an association that is consistent in magnitude and direction, there may be sufficient evidence for an association. There is sufficient evidence of an association between exposure to herbicides and the following health outcomes:

Soft-tissue sarcoma
Non-Hodgkin's lymphoma
Hodgkin's disease
Chloracne

Limited/Suggestive Evidence of an Association

Evidence is suggestive of an association between herbicides and the outcome but is limited because chance, bias, and confounding could not be ruled out with confidence. For example, at least one high-quality study shows a positive association, but the results of other studies are inconsistent. There is limited/suggestive evidence of an association between exposure to herbicides and the following health outcomes:

Respiratory cancers (lung, larynx, trachea)
Prostate cancer
Multiple myeloma
Acute and subacute peripheral neuropathy (new disease category)
Spina bifida (new disease category)
Porphyria cutanea tarda (category change in 1996)

Inadequate/Insufficient Evidence to Determine Whether an Association Exists

The available studies are of insufficient quality, consistency, or statistical power to permit a conclusion regarding the presence or absence of an association. For example, studies fail to control for confounding, have inadequate exposure assessment, or fail to address latency. There is inadequate or insufficient evidence to determine whether an association exists between exposure to herbicides and the following health outcomes:

Hepatobiliary cancers
Nasal/nasopharyngeal cancer
Bone cancer
Female reproductive cancers (cervical, uterine, ovarian)
Breast cancer
Renal cancer
Testicular cancer
Leukemia
Spontaneous abortion

[1-6]

Birth defects (other than spina bifida)
Neonatal/infant death and stillbirths
Low birthweight
Childhood cancer in offspring
Abnormal sperm parameters and infertility
Cognitive and neuropsychiatric disorders
Motor/coordination dysfunction
Chronic peripheral nervous system disorders
Metabolic and digestive disorders (diabetes, changes in liver enzymes, lipid abnormalities, ulcers)

Immune system disorders (immune suppression and autoimmunity)
Circulatory disorders
Respiratory disorders
Skin cancer (category change in 1996)

Limited/Suggestive Evidence of No Association

Several adequate studies, covering the full range of levels of exposure that human beings are known to encounter, are mutually consistent in not showing a positive association between exposure to herbicides and the outcome at any level of exposure. A conclusion of "no association" is inevitably limited to the conditions, level of exposure, and length of observation covered by the available studies. *In addition, the possibility of a very small elevation in risk at the levels of exposure studied can never be excluded.* There is limited/suggestive evidence of *no* association between exposure to herbicides and the following health outcomes:

Gastrointestinal tumors (stomach cancer, pancreatic cancer, colon cancer, rectal cancer)
Bladder cancer
Brain tumors

NOTE: "Herbicides" refers to the major herbicides used in Vietnam: 2,4-D (2,4-dichlorophenoxyacetic acid); 2,4,5-T (2,4,5-trichlorophenoxyacetic acid) and its contaminant TCDD (2,3,7,8-tetrachlorodibenzo-*p*-dioxin); cacodylic acid; and picloram. The evidence regarding association is drawn from occupational and

other studies in which subjects were exposed to a variety of herbicides and herbicide components.

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[7-42]

Summary

Most of the agricultural studies indicate some elevation in risk of prostate cancer. One large, high-quality study in farmers showed an increased risk, and subanalyses in this study indicated that the increased risk is specifically associated with herbicide exposure (Morrison et al., 1993). In addition, a significantly increased risk of prostate cancer was observed in both white and nonwhite farmers in another large study (Blair et al., 1993). The three major studies of production workers (Fingerhut et al., 1991; Manz et al., 1991; Saracci et al., 1991) showed a small, but not statistically significant, elevation in risk. In the NIOSH study, the subcohort with at least 20 years latency and [7-43] at least one year of exposure had a slightly increased risk, (SMR=1.5, CI 0.7-2.9) (Fingerhut et al. 1991). Most of the studies used mortality as an outcome, so detection bias is not likely to explain these results. It should be noted, however, that most of the associations are relatively weak (RR<1.5). Most Vietnam veterans have not yet reached the age when this cancer tends to appear. Results are summarized in Table 7-5.

Conclusions

There is limited/suggestive evidence of an association between exposure to the herbicides (2,4-D, 2,4,5-T and its contaminant, TCDD; cacodylic acid; and picloram) and prostate cancer. The evidence regarding association is drawn from occupational and

other studies in which subjects were exposed to a variety of herbicides and herbicide components.

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